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#10

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/881,393	06/24/97	FODSTAD	0 7885-33USD1

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EXAMINER	
CHIN,C	
ART UNIT	**PAPER NUMBER**
1641	10

DATE MAILED: 07/12/99

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
08/881393	Fodstad et al
Examiner	**Group Art Unit**
C. Chin	1641

—The MAILING DATE of this communication appears on the cover sheet beneath the correspondence address—

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, such period shall, by default, expire SIX (6) MONTHS from the mailing date of this communication .
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

☒ Responsive to communication(s) filed on 3/19/99.

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 1 1; 453 O.G. 213.

Disposition of Claims

☒ Claim(s) 17-42 is/are pending in the application.

Of the above claim(s) 34-37, 39, 40 is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 17-33, 38, 41-42 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☒ Claim(s) 17-42 are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119 (a)-(d)

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 11 9(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 1 7.2(a)).

*Certified copies not received: _____.

Attachment(s)

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☒ Notice of Reference(s) Cited, PTO-892

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Interview Summary, PTO-413

☐ Notice of Informal Patent Application, PTO-152

☐ Other _____

Office Action Summary

DETAILED ACTION

Election/Restriction

1. Applicant's election with traverse of cancer cells of the gastrointestinal tract as an antigen as recited in claim 38 in Paper No. 9 is acknowledged. The traversal is on the ground(s) that there is no undue burden on the Examiner. This is not found persuasive because the search involved for each of the species requires a different search strategy in terms of classes, subclasses, and different key word search terms on commercial data bases.

The requirement is still deemed proper and is therefore made FINAL.

Claims 34, 35, 36, 37, 39, and 40 are non-elected claims.

Claim Rejections - 35 U.S.C. § 112

2. Claims 17-33, 39, and 41-42 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 17 is vague. The preamble is not consistent with the body of the claim. The preamble recites a method for detection of specific target cells but the last step of the claim is directed to the counting of target cells.

Claim Rejections - 35 U.S.C. § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. Claims 17-33 and 41 are rejected under 35 U.S.C. 103(a) as being unpatentable over .

Widder et al (EP 016,552) teach a method for separation of selected population of cells from a mixed cell population using magnetic particles coated with a layer of specific antibodies which selectively bind to the select population. The coated microspheres with antibodies specific to target cells are contacted with the mixed population and the bound select population is magnetically separated from the mixed population (page 4). The magnetically responsive microspheres have protein A associated into the surface which selectively binds antibodies through the Fc region of the antibodies so that Fab arms of the antibodies extend outwardly for binding (page 4). Widder et al teach microspheres which are coupled with FITC conjugated rabbit IgG by incubation at 37 degrees Celsius for 20 minutes and examined (page 10, Example 1). Furthermore, Widder et al teach using the coated particles to separate red blood cells (RBC) from suspensions containing a mixture of different RBCs. Antibodies were coupled to the microspheres by incubation of 0.5 mg of the microspheres suspended in 0.2 ml of 0.9% NaCl solution containing 0.1% Tween 80 (polyethylene sorbitans monoleate). The RBCs were labeled with ^{51}Cr

and incubated with mild agitation and bound microspheres were separated and counted using a gamma counter (page 11, Example 2).

The method of Widder et al differs from the instant invention in failing to teach incubation of the antibody coated microspheres in mild detergent for 5-10 minutes to 2 hours at 4 degrees Celsius. Furthermore, Widder fails to teach the use of an antibody to immobilize antibodies on the surface of the magnetic particles.

Connelly et al teach various fixatives used to fix cells without destroying cellular properties. Connelly et al specifically teach fixing cells with phosphate buffer solution followed by DMSO and DNBS, Tween 20 or Tween 80, and formaldehyde (col. 9, lines 10-14) and then incubating the cells for 20 minutes to 2 hours at temperatures ranging from 0-37 degrees Celsius (col. 9, lines 20-48).

It would have been obvious to one of ordinary skill in the art to immobilize other antibodies on the surface of the magnetic particles in the method of Widder et al because such method of immobilizing antibodies on the surface of a solid support, such as magnetic particles, is conventional and well known in the art. It would have been obvious to one of ordinary skill in the art use detergents to treat cells used by Connelly following certain specific temperature and time parameters because the use of detergents to treat cells is well known and conventional in the art for removing extraneous matter from the cells that will interfere with assays. It also would have been obvious to one of ordinary skill in the art to incorporate Connelly's fixative technique and parameters in the Widder's separation method because Connelly specifically states that one of

ordinary skill in the art of cell fixation may routinely have to vary the aforementioned cell treatment parameters in order to obtain desired cell fixation without substantial destruction of cellular properties.

With respect to claim 41, it would have been obvious to one of ordinary skill in the art to place the reagents used in the method of Widder et al, as modified by Connelly, in a kit arrangement because kits are well known in the art for their recognized advantages of convenience and economy.

5. Claims 17-33, 38, and 41-42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Widder et al in view of Kemmer et al and Terasaki et al.

See above for the teachings of Widder et al.

The method of Widder et al differs from the instant invention in failing to teach separation of cancer cells.

Kemmer et al teach isolation of tumor cells from a mixed cell suspension of human tumor tissue which contains tumor cells, leukocytes, and erythrocytes, using magnetic beads coated with monoclonal antibodies.

Terasaki et al (U.S. Patent 4,752,569) teach the preparation of monoclonal antibodies for use in the diagnosis of neoplastic conditions, with a wide variety of different tumors. The hybridoma producing the monoclonal antibodies can also be used for transforming other cells to make them monoclonal antibody producing or as a source of the gene expression of the

immunoglobulin. The entire antibody need not be used but rather only fragments such as Fab, $(Fab')_2$, etc. Terasaki et al teach incorporation of monoclonal antibodies into reagents for use in detection methods. The monoclonal antibodies may be labeled with enzymes such as horseradish peroxidase and conjugated covalently or non-covalently with other antibodies or with magnetic particles for use in diagnostic assays.

It would have been obvious to one of ordinary skill in the art to use the method of Widder et al to separate cancel cells from a variety of cells, as taught by Kemmer et al, because Kemmer et al teach that cancer cells can be separated from a mixed population of cells by an immunological magnetic process such as the method taught by Widder et al and Widder et al is not limiting with respect to the types of cells that can be separated with their disclosed method. It also would have been obvious to one of ordinary skill in the art to use the cancer cell specific antibodies of Terasaki et al in the method of Widder et al, as modified by Kemmer et al, because the choice of cells to be separated dictate the choice of antibodies to be used, i.e. one would use cancer cell antibodies if the cells that are to be separated are cancer cells.

With respect to claims 41-42, it would have been obvious to one of ordinary skill in the art to place the reagents used in the method of Widder et al, as modified by Kemmer et al and Teraski et al, in a kit arrangement because kits are well known in the art for their recognized advantages of convenience and economy.

Conclusion

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chris Chin whose telephone number is (703) 308-3991. The examiner can normally be reached on Monday-Thursday from 8:30 am to 6:00 pm. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel, can be reached on (703) 308-4027. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

cchin/cc
June 6, 1999

Christopher L. Chin

CHRISTOPHER L. CHIN
PRIMARY EXAMINER
GROUP ~~1800~~ 1641